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EDITORIAL

Delirium in the Cardiac Patient

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Introduction

The Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5) [1] defines delirium as a disturbance in attention and awareness that develops over a short period and involves fluctuation in severity. This profile is also accompanied by an additional disturbance in cognition (e.g., memory), which are not explained by a preexisting neurocognitive disorder. Arousal levels, such as those in patients in a coma, must also not be severely reduced. Finally, to make the diagnosis of delirium, there must be evidence that the disturbance is a direct physiological consequence of another medical condition, substance intoxication or withdrawal, exposure to a toxin, or due to multiple etiologies.

Delirium Types

The three recognized clinical subtypes of delirium are 1) hyperactive, 2) hypoactive, and 3) mixed [2]. Patients with hyperactive delirium exhibit increased psychomotor activity, such as rapid speech, irritability, and restlessness. They may be challenging to manage, removing lines, getting out of bed, attempting to leave the hospital, or even becoming violent. Patients with hypoactive delirium exhibit psychomotor retardation, with symptoms such as lethargy, slowed speech, apathy, and decreased alertness. Because these patients do not create disturbances, they may be less likely to be recognized as delirious without active monitoring [3]. Patients with mixed delirium shift between hyperactive and hypoactive states. This shift between states, especially from hyperactive to hypoactive, may give staff the false impression that the patient's condition has improved when it actually has worsened. Recognition of hyperactive and hypoactive delirium states is critical to achieve prompt, effective management of the underlying delirium etiology.

Importance of Recognition

Delirium is common in patients undergoing cardiac surgery; with estimates ranging from 26% to 52% [4]. In cardiac intensive care units, patients with delirium have more extended hospital and ICU stays; increased healthcare costs; and greater morbidity, mortality, and risk of cognitive decline [4]. Additionally, the duration of delirium is an independent risk factor for worse cognition at long-term follow-up over 1 year [5]. When delirium is recognized, tailored work-up and intervention for the underlying cause can reduce the duration of delirium and its negative consequences.

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Presentation

Delirium can present in various ways, with features that overlap with other conditions such as dementia, depression, mania, or personality disorders. This similarity can lead to misdiagnosis, thus highlighting the importance of understanding the diverse presentations of delirium.

Dementia typically has a slow and progressive onset, with cognition worsening over months to years, without noticeable changes or fluctuations from day to day. In most cases of dementia, such as those due to Alzheimer's disease, simple attention (the ability to focus on a stimulus while ignoring distraction) is not significantly impaired until late in the disease course. Individuals experiencing psychosis due to mania or depression typically undergo gradual worsening of symptoms over days to weeks, or even months. These individuals, compared with those with delirium, typically exhibit less fluctuation in symptoms and arousal levels throughout the day, and their mood-associated symptoms are more prominent. In contrast, delirium has an acute onset, typically over hours to several days; inattention is a major symptom, and mental status and arousal often fluctuate. This acute and rapidly changing presentation distinguishes delirium from the more gradual and stable progression seen in dementia and certain mood disorders.

When discussing delirium in cardiac patients, considering specific diagnoses is essential. Heart failure can predispose patients to delirium, and some studies have reported an incidence as high as one in three patients [6]. This may be due to cerebral hypoperfusion and low cardiac output, as indicated by elevated B-type natriuretic peptide levels in patients with delirium. Patients undergoing transcatheter aortic valve replacement are at high risk of delirium, probably because of the concurrent vascular disease often observed in patients with aortic stenosis [7]. Additionally, ischemic brain injury triggered by emboli from valve particles or aortic plaque dislodgment during the procedure may contribute [8]. Notably, cerebral embolic protection strategies for surgical aortic valve replacement have been reported to decrease the incidence of delirium [9].

Risk Factors

Several risk factors contribute to the development of delirium, which can be categorized into 1) preexisting conditions, 2) factors related to the patient's current illness, and 3) hospital-related factors [10]. These factors can combine to trigger and exacerbate delirium.

Common patient characteristics that increase the risk of delirium include:

1. Advanced age
2. Dementia
3. Low educational level
4. High comorbidity burden
5. Frailty
6. Visual and hearing impairment
7. Depression
8. Alcohol abuse
9. Poor nutrition
10. Illicit drug, opioid, or benzodiazepine use

A history of previous delirium episodes is also a risk factor.

In cardiac patients, specific factors related to their current illness, such as cardiovascular and aortic surgery, can elevate the risk of delirium. Additionally, acute infection, dehydration, electrolyte imbalance, acute kidney injury, and heart failure are common in cardiac patients and can contribute to delirium.

Factors like the failure of non-invasive ventilation or prolonged ventilation exceeding 96 hours are associated with a higher risk of delirium for intensive care patients.

After admission to the hospital or ICU, various post-admission factors can further precipitate delirium. These factors include:

1. Pain
2. Infection
3. Use of invasive devices
4. Immobility
5. Metabolic imbalances
6. Polypharmacy
7. Sleep deprivation
8. Environmental conditions
9. Certain medications

Regarding cardiac patients, the aging process leads to vascular changes that may decrease reduce cerebral blood flow; consequently, making older patients more sensitive to oxygen variations. Because the brain heavily relies on oxygen and glucose, misdirected blood flow can lead to an oxygen-demand mismatch, potentially triggering delirium [11].

Cardiovascular medications have been associated with delirium. Some studies have suggested an association between digoxin use and an elevated delirium risk, particularly among older adults. Certain antiarrhythmic medications, such as amiodarone, have been associated with delirium, particularly in older patients or those with multiple comorbidities. Although beta-blockers are usually well-tolerated, they have been implicated in some cases of delirium, particularly in older individuals [12].

Screening Tools

Healthcare professionals operating without a standardized method for detecting delirium are unlikely to make the delirium diagnosis; the sensitivity of "clinical impression" in the ICU setting has been reported to be 29% [13]. Prompt recognition and management of delirium require consistent, systematic screening [14]. The Confusion Assessment Method (CAM), administered by a specially trained healthcare provider, is the gold standard in research settings [15, 16]. However, this assessment is relatively time-consuming, requiring at least 10 minutes to administer, and is not designed for implementation by nursing staff. Therefore, additional screening tools have been developed for practical use across clinical settings.

Several delirium assessments have been developed for the ICU setting [13]. One of the most widely used methods, the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU), is a rapid (approximately 2 minutes for administration), straightforward, and effective means for nursing staff to screen for delirium in the ICU [17, 18]. First, patients are scored with the Richmond Agitation and Sedation Scale (RASS); if the level of arousal is greater than −4 (deep sedation), patients are assessed for delirium. A diagnosis of delirium requires the following: 1) acute change from mental status baseline or mental status fluctuation during the prior 24 hours, 2) inattention, measured as errors when the patient is asked to squeeze the examiner's hand when they hear the letter "A," and 3) altered level of consciousness (RASS score other than 0, alert and calm) or disorganized thinking, as measured by errors on a set of yes or no questions and commands. Detailed free instructions are available at https://www.icudelirium.org/medical-professionals/delirium/monitoring-delirium-in-the-icu.

Although the CAM-ICU has been applied across care settings, it may be less sensitive to mild delirium [19]. Therefore, other methods may be more effective outside critical care units. Many screening tools have been developed and validated, each with relative advantages and disadvantages, across hospital settings. Among them, the Ultra Brief CAM (UB-CAM) is a fast (1–3 minutes), sensitive (93%) screening method [20]. Detailed free instructions are available at https://deliriumnetwork.org/measurement/ub-cam/. Unfortunately, regardless of the screening tool used, premorbid cognitive impairment can mimic the symptoms of delirium and create a dilemma for clinicians. For patients undergoing cardiac operations, preoperative baseline use of screening tools, where practical, can enable more accurate identification of postoperative delirium.

Management of Delirium

Delirium management strategies are based on expert opinions, best practices, and observational studies. Conducting controlled trials is difficult in patients with cognitive impairment; consequently, most available evidence is from observational studies. The most important means of delirium management is prevention through nonpharmacological, multi-modal methods in high-risk patients [21, 22].

Prevention

Although no single intervention or group of interventions can always prevent delirium, focusing on modifiable risk factors can decrease the incidence of delirium [23]. Nonpharmacological multicomponent delirium prevention efforts have been shown to decrease delirium incidence by 44% and decrease the risk of falls by 64%; therefore, these methods should be the mainstay of delirium management [21]. Other delirium prevention methods such as "4M" (What Matters, Medication, Mentation, and Mobility) can be implemented as a standard delirium prevention bundle [24]. No proven medical therapies are available for delirium prevention.

Treatment

Delirium is treated by diagnosis and treatment of its underlying cause. A thorough medication history is essential, because many medications can precipitate delirium, particularly in high-risk patients. Benzodiazepines are particularly concerning and should be avoided in patients at high risk of delirium. Benzodiazepines should be used in patients with delirium only in the treatment of alcohol withdrawal [12]. Other particularly concerning medications are opioids, dihydropyridines, and antihistamines [12]. These medications, particularly dihydropyridines, are often used in patients with cardiac conditions and consequently should be used with caution in patients at high risk of delirium. The first-line approach to treating delirium in cardiac patients is to remove medications that might be precipitating delirium.

Metabolic disturbances, such as derangements in sodium calcium, should be assessed and treated. Hypoglycemia and hyperglycemia both have effects on brain function, and should be evaluated and treated appropriately. Both dehydration and over-hydration can lead to delirium, particularly in older people. Thus, clinicians face a particular challenge with cardiac patients in whom volume overload is being treated; a delicate balance must be struck to ensure that the patients remain adequately hydrated. Any urinary catheters, indwelling lines, or tethers should be assessed for necessity and removed if possible. Infection, particularly urinary tract infection or pneumonia, can cause delirium and should be considered in the differential diagnosis. Mobility is essential, as is improving environmental stimuli. Cardiac patients may be placed on bed rest or in an intensive care setting. Both immobility and over-stimulation can worsen delirium. Finally, pain should be assessed and adequately treated, preferably with multi-modal treatment and non-opiate approaches [25].

No proven pharmacological therapy is available for delirium. Trials investigating cholinesterase inhibitors (e.g., donepezil and rivastigmine) have indicated no effects [26]. Dexmedetomidine administration may show promise for the management and prevention of delirium in postoperative and critical care, although studies have reported mixed results. In one randomized trial, the use of low dose dexmedetomidine has been associated with a diminished incidence of postoperative delirium [27]. However, not all studies have consistently replicated these findings [28]. Dexmedetomidine's adverse effects are similar to those of clonidine, and encompass bradycardia and hypotension associated with dose, thus limiting its application in many cardiac patients.

Despite their long history of use for management of behavioral symptoms in delirium, because of their sedative effects, benzodiazepines can exacerbate delirium and are not clinically indicated except in patients with alcohol withdrawal [29]. Antipsychotic agents have been traditionally used for behavioral management, but trials have shown that, in both hypoactive and hyperactive delirium, typical and atypical antipsychotics do not perform better than placebo regarding any studied outcome, including delirium-free days, survival, rates of rescue medication, or rates of restraint [30]. The American Geriatrics Society has stated that: "The prescribing practitioner should not prescribe antipsychotic medications for the treatment of older adults with postoperative delirium who are not agitated and threatening substantial harm to self or others." Notably, intravenous haloperidol has an FDA black box warning because of QT-prolongation; therefore, if prescribed, EKG monitoring is required. Unfortunately, medications prescribed in the hospital are often continued after discharge, and long-term use of antipsychotic agents in patients with dementia increase mortality and should be avoided. Restraints are appropriate only in the event of behaviors that pose a risk to life or necessary for medical care, because restraints are associated with a fourfold increase in the risk of delirium [10].

Conclusion

Delirium is a major source of morbidity and mortality, particularly in cardiac patients. Screening is critical for early identification and treatment of the underlying causes. Pharmacological methods are used to prevent patients from harming themselves or others, but these methods do not improve or treat the underlying cause of delirium, or improve patient outcomes. The mainstay of delirium management is prevention.

Conflicts of Interest

The authors declare no conflicts of interest.

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